UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/550,866	09/23/2005	Dimitrios T Drivas	MP-02	1389

50446 7590 05/14/2008
HOXIE & ASSOCIATES LLC
75 MAIN STREET , SUITE 301
MILLBURN, NJ 07041

EXAMINER	
MERTZ, PREMA MARIA	
ART UNIT	PAPER NUMBER
1646	
MAIL DATE	DELIVERY MODE
05/14/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/550,866	DRIVAS ET AL.	
	Examiner	Art Unit	
	Prema M. Mertz	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 April 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16* is/are pending in the application.

4a) Of the above claim(s) *3-6 and 10-15* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-2, 7-9, 16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-2, 7-9 have been amended (4/14/2008) and together with new claim 16 (4/14/2008) are under consideration. Claims 3-6, 10-15 are withdrawn from consideration by the Examiner as drawn to non-elected claims.

2. Receipt of Applicant's arguments and amendments filed on 4/14/2008 is acknowledged.

3. The following previous rejections and objections are withdrawn in light of applicants amendments filed on 2/20/07:

(i) the objection to the specification, i.e. the title of the invention;

(ii) the rejection of claims 7-9, under 35 USC 112, first paragraph, for lack of adequate written description;

(iii) the rejection of claims 1-2, 7-9, under 35 U.S.C. 112, second paragraph.

Applicant's arguments with respect to claims 1-2, 7-9, have been considered but are moot in view of the new ground(s) of rejection over claims 1-2, 7-9, 16.

4. Applicant's arguments filed on 4/14/2008 have been fully considered but were persuasive in part. The issues remaining and new issues are stated below.

Claim Rejections - 35 USC § 112, first paragraph, scope of enablement

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5a. Claims 1-2, 7-9, 16, are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating allergy comprising administering at

least one of the eotaxin peptides set forth in SEQ ID NOs: 1-38, 42-61, 117-121 and 130-132, and at least one of the IL-5 peptides set forth in SEQ ID NOs: 62-116 and 122-123, does not reasonably provide enablement for a method for treating asthma by administering two or more cytokines as recited in claim 1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

This rejection is maintained for reasons of record set forth at pages 3-9 of the previous Office action (10/12/07).

Applicants argue that the clams as amended specifically recite that the condition to be treated is asthma and the targets of the immunization are specific cytokines, e.g., eotaxin and IL-5. Applicants also argue that the use of vaccines to generate antibodies is a mature art, so that the guidance required for enablement is not that great, and that the specification moreover provides a highly detailed teaching in the selection of immunogenic fragments of the target cytokines, effective conjugates and methods for making conjugates, effective adjuvants, and optimal formulations. However, contrary to Applicants arguments, amended claim 1 recites "at least two different Th2 cytokines (or peptide fragments thereof) selected from the group consisting of eotaxin, eotaxin-2, eotaxin-3, IL-4, IL-5, IL-9, and IL-13". The issue here is that Applicants are claiming a method of treating asthma by administering cytokine peptide fragments which have not been previously disclosed in the prior art. Applicants argue that the Federal Circuit in *Falko-Gunter Falkner v. Inglis*, 448 F.3d 1357 (Fed. Cir 2006) emphasized that the existence of publications which disclosed poxvirus essential genes was sufficient to provide enablement for the claims of the application even though such genes were not disclosed

specifically in the application. However, contrary to Applicants arguments that the Examiner is requiring clinical data on the peptide fragments and that the standard is that routine experimentation is required to identify the numerous embodiments (cytokine peptide fragments) is a position that has been routinely dismissed by the courts, as shown by the CAFC decision in Genentech, Inc. v. Novo. Nordisk, 42 USPQ2d, 100 (CAFC 1997), in which the decisions in In re Fisher, Amgen Inc. V. Chugai Pharmaceuticals Co. Ltd., and In re Wands were considered as the controlling precedents in determining enablement issues where protein and recombinant DNA issues are concerned. These decisions have been relied upon in the instant rejection and by the Court because they show that the judicial interpretation of the first paragraph of 35 U.S.C. § 112 requires that the breadth of claims must be based upon the predictability of the claimed subject matter and not on some standard of trial and error. To argue that one can make material embodiments of the invention and then test for those that work in the manner disclosed or that the instant claims only encompass the working embodiments is judicially unsound. Unless one has a reasonable expectation that any one material embodiment of the claimed invention would be more likely than not to function in the manner disclosed or the instant specification provides sufficient guidance to permit one to identify those embodiments which are more likely to work than not, without actually making and testing them, then the instant application does not support the breadth of the claims.

Further, In re Wands determined that the repetition of work which was disclosed in a patent application as producing a composition containing an antibody, which is a naturally-occurring compound, did not constitute undue experimentation even if the antibody produced thereby was not identical to those that were disclosed in that application. The instant claims are

not limited to naturally-occurring compounds and the instant specification does not provide a description of a repeatable process of administering peptide fragments of eotaxin, eotaxin-2, eotaxin-3, IL-4, IL-5, IL-9, and IL-13 for treating asthma. To practice the instant invention in a manner consistent with the breadth of the claims would not require just a repetition of the work that is described in the instant application but a substantial inventive contribution on the part of a practitioner which would involve the determination of those amino acid residues of the seven disclosed naturally-occurring proteins, which are required for functional and structural integrity of those proteins. It is this additional characterization of the seven disclosed proteins that is required in order to obtain the structural data needed to permit one to produce the claimed peptides to be administered in the claimed method that constitutes undue experimentation.

The recitation of "peptide fragments" in claim 1, is not commensurate with the scope of the specification. Given the breadth of claim 1 in light of the predictability of the art as determined by the number of working examples, the level of skill of the artisan, and the guidance provided in the instant specification and the prior art of record, it would require undue experimentation for one of skill in the art to practice the claimed invention.

Claim Rejections - 35 U.S.C. § 112, second paragraph

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-2, 7-9, and 16, are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1, line 3, is vague and indefinite because it recites "(or peptide fragments thereof)". It is suggested that brackets be deleted because the limitation appears confusing.

Claim 1, line 7, is vague and indefinite because it recites "derived". This limitation is unclear because it is unclear how the immunogenic carrier can be "derived" from one or more of protein toxoids, keyhole limpet hemocyanin (KLH), influenza virus haemaglutinin, Bacille Calmette Guerin (BCG), and ovalbumin (OVA).

Similarly, claim 7, line 5, recites "derived" from diphtheria toxoid or tetanus toxoid. This limitation is unclear because it is unclear how the immunogenic carrier can be "derived" from diphtheria toxoid or tetanus toxoid.

Claim 16, line 1, is vague and indefinite because it recites "of peptide fragment" rather than "or peptide fragment".

Claim 16 recites the limitation "peptide fragment" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claim 16 recites the limitation "peptide fragment" in line 4. There is insufficient antecedent basis for this limitation in the claim.

Claims 2, 8-9, are rejected as vague and indefinite insofar as they depend on the above rejected claims for their limitations.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in Graham v. John Deere Co., 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

7a. Claims 1-2, 7-9, are rejected under 35 U.S.C. 103(a) as unpatentable over WO 03/040164 ('164, priority date 11/7/2002) in view of the Cutler et al. patent (U.S. Patent No. 6,309,642).

The '164 reference teaches a composition comprising a virus-like particle and at least one protein or peptide of IL-5, IL-13 and/or eotaxin bound thereto (see abstract; page 9 [0020]). The reference also teaches that the compositions are useful in the production of vaccines for the treatment of allergic diseases and to induce self-specific immune responses by administering virus-like particles with a peptide of IL-5, IL-13 or eotaxin (see abstract; pages 112-113; page 125). The reference does not teach administering both the IL-5 and eotaxin cytokine proteins or peptides coupled to an immunogenic carrier like KLH or tetanus toxoid to induce autoantibodies for the treatment of an allergic disease like asthma.

Cutler et al teaches coupling peptide sequences, with potential vaccine and therapeutic application, to immunogenic carrier proteins such as KLH or tetanus toxoid to induce production of antibodies (see column 16, lines 40-51).

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art to modify the method of '164 such that it includes administering IL-5 with eotaxin as taught by '164, each cytokine coupled to an immunogenic carrier such as KLH or tetanus toxoid as taught by Cutler to obtain the known functions and advantages of IL-5 and eotaxin since '164 teaches the production and administration of virus-particles with both these cytokines to induce the production of antibody responses to these cytokines involved in inflammation. One of ordinary skill in the art would have been motivated to do so because the '164 patent teaches the production of vaccines with each of these components and Cutler teaches the advantages of coupling immunogenic carriers to peptides. Thus the artisan would have expected equal success using both cytokine components together to obtain a synergistic effect. To combine two compositions each of which is taught by the prior art to be useful for same purpose in order to form third composition that is to be used for very same purpose would have been obvious to one of ordinary skill in the art at the time the invention was made. The combination would have been obvious to the skilled artisan and the results achieved would have been expected (In re Kerkhoven, 205 USPQ 1069). Therefore, the combined teachings of WO 03/040164 and Cutler et al. patent (U.S. Patent No. 6,309,642) render obvious claims 1-2, 7-9.

Applicants argue that there is no teaching in the '164 application to combine vaccination there is no teaching in the ' 164 application to combine vaccination for multiple cytokines, e.g.,

eotaxin and IL-5 and there is likewise no teaching to use immunogenic carriers other than virus-like particles. However, contrary to Applicants arguments, if the '164 reference taught a method of administering both IL-5 and eotaxin coupled to an immunogenic carrier, this rejection would be a 35 USC 102(b) rejection rather than a 35 USC 103 rejection.

7b. Claims 1-2, 7-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 00/65058 ('058) in view of the Ponath et al. patent (U.S. Patent No. 7,265,201) and further in view of Cutler et al. (U.S. Patent No. 6,309,642).

'058 discloses treating conditions such as asthma by downregulating IL-5 by enabling the production of antibodies against IL-5 by administering to a subject variants of IL-5 to induce production of cross-reactive antibodies capable of binding to autologous IL-5 (see abstract). However, the reference does not teach administering eotaxin to induce the production of anti-eotaxin antibodies to treat asthma or eotaxin coupled to an immunogenic carrier like KLH or tetanus toxoid to induce autoantibodies for the treatment of an allergic disease like asthma.

Ponath et al. teaches administering peptides of eotaxin to be administered for immunization in the treatment of allergic conditions such as asthma(see abstract; column 13, lines 6-14; column 14, lines 13-24). However, the reference does not teach administering IL-5 to induce the production of anti-IL-5 antibodies to treat asthma or IL-5 coupled to an immunogenic carrier like KLH or tetanus toxoid to induce autoantibodies for the treatment of an allergic disease like asthma.

Cutler et al teaches coupling peptide sequences, with potential vaccine and therapeutic application, to immunogenic carrier proteins such as KLH or tetanus toxoid to induce production of antibodies (see column 16, lines 40-51).

Therefore, it would have been *prima* facie obvious to one having ordinary skill in the art at the time the invention was made, to modify the method of WO 00/65058 ('058) comprising administering an IL-5 composition and a composition comprising eotaxin as taught by Ponath et al such that it includes coupling both cytokines to immunogenic carriers like KLH or tetanus toxoid as taught by Cutler et al, to obtain the known functions and advantages of IL-5 and eotaxin and to increase the vaccine and therapeutic potential of both cytokines. One of ordinary skill in the art would have been motivated to do so because both references teach the production of vaccines with each of these components. Thus the artisan would have expected equal success using both components together to obtain a synergistic effect. To combine two compositions each of which is taught by the prior art to be useful for same purpose in order to form third composition that is to be used for very same purpose would have been obvious to one of ordinary skill in the art at the time the invention was made. The combination would have been obvious to the skilled artisan and the results achieved would have been expected (In re Kerkhoven, 205 USPQ 1069). Therefore, the combined teachings of WO 03/040164, Ponath et al (U.S. Patent No. 7,265,201), and Cutler et al. patent (U.S. Patent No. 6,309,642) render obvious claims 1-2, 7-9.

Applicants argue that the '058 application discloses fusion peptides to raise an antibody response to IL-5, it does not disclose combination vaccines, nor does it disclose the immunogenic conjugates as claimed. Applicants argue that Ponath discloses eotaxin and

methods of making antibodies to eotaxin. These antibodies are said to have utility in as drugs or in diagnostic or in vitro applications, but Ponath does not disclose therapeutic vaccines, let alone methods utilizing combinations of therapeutic vaccines. Furthermore, Applicants argue that the Supreme Court in *KSR Int'l., Co. v. Teleflex, Inc.,* 127 S. Ct. 1727, 1735 (2007) (citing *Graham v. John Deere Co.,*383 US 1, 17-18 (1966)) recognized that a showing of "teaching, suggestion, or motivation" to combine prior art could provide a helpful insight in determining whether the claimed subject matter is obvious under 35 USC 103(a). *Id.* at 1741. The Supreme Court specifically stated that "it will be necessary.., to determine whether there was an apparent reason to combine [or modify] the known elements [in the prior art] in the fashion claimed by the patent at issue. To facilitate review, this analysis should be made *explicit."* Id. at 1740 - 41 (emphasis added). However, contrary to Applicants arguments, the Court in *KSR* held that "Neither §103's enactment nor *Graham's* analysis disturbed the Court's earlier instructions concerning the need for caution in granting a patent based on the combination of elements found in the prior art." *KSR v. Teleflex*, 550 U.S., 82 USPQ2d 1385, 1389 (2007). The *KSR* court stated that "a combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results." *KSR* at 1389.

Furthermore, the KSR court concluded that "obvious to try" may be an appropriate test under 103. The Supreme Court stated in *KSR*

When there is motivation

"to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to anticipated success, it is likely the product is not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to

try might show that it was obvious under § 103." *KSR Int'l Co. v. Teleflex Inc.,* 127 S. Ct. 1727,__, 82 USPQ2d 1385, 1397 (2007).

In the instant case '058 discloses treating conditions such as asthma by downregulating IL-5 by enabling the production of antibodies against IL-5 by administering to a subject variants of IL-5 to induce production of cross-reactive antibodies capable of binding to autologous IL-5 (see abstract). Ponath et al. teaches administering peptides of eotaxin to be administered for immunization in the treatment of allergic conditions such as asthma (see abstract; column 13, lines 6-14; column 14, lines 13-24). The claims would have been obvious in view of the prior art references because one of ordinary skill in the art would have been motivated to combine the compositions because both references teach the production of vaccines with each of these components. Thus the artisan would have expected equal success using both components together to obtain a synergistic effect and the resulting method would have yielded predictable results to one of ordinary skill in the art at the time of the invention. From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *primafacie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

Conclusion

No claim is allowed.

Claims 1-2, 7-9, and 16, are rejected.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Prema Mertz whose telephone number is (571) 272-0876. The examiner can normally be reached on Monday-Friday from 7:00AM to 3:30PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, can be reached on (571) 272-0835.

Official papers filed by fax should be directed to (571) 273-8300. Faxed draft or informal communications with the examiner should be directed to (571) 273-0876.

Information regarding the status of an application may be obtained from the Patent application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Prema Mertz/
Primary Examiner
Art Unit 1646